

Shchukina, M. N.

✓ Imidazole series. 11. Action of α -halo ketones on 2-
mercaptoimidazoles. M. Kochergin and M. N. Shchukina
(S. Ordzhonikidze All-Union Chem. Philm. Ser.
Research Inst. Moscow), Zhur. Obshchel Khim. 26, 458-
66(1956); cf., CA 50, 9387i. — The cyclization of 4(5)-
phenyl-2- β -oxoalkylmercaptoimidazoles to imidazo[2,1-b]-
thiazoles is catalyzed by H ions. A soln. of 1.3 g. Na, 100
ml. 96% EtOH and 10 g. 4(5)-phenyl-2-mercaptoimidazole
was heated 1.2 hrs. with 7.9 g. 2-chlorocyclohexanone at 65-
66° (finally at reflux) yielding 97.7% 4(5)-phenyl-2-(2-cyclo-
hexan-1-yl)mercaptoimidazole (I), m. 123-4° (from EtOH).
The action of appropriate halo ketones similarly yielded the
following 2- β -oxoalkylmercapto-4(5)arylimidazoles (β -oxoalkyl
group and aryl group shown, resp.): AcCH₂, Ph, 94.8%, m.
120-1° (HCl salt, m. 153°; semicarbazone, m. 148-8°);
AcCHMe, Ph, 86.3%, m. 96-7° (HCl salt, m. 177-8°);
BzCH₂, Ph, 98.8%, m. 135-6° (HCl salt, m. 220-2°; HBr
salt, m. 226-7°; semicarbazone, m. 179-81); p -O₂NC₆H₄-
COCH₃, Ph, 96.7%, m. 155°; m -O₂NC₆H₄COCH₃, Ph,
97.6%, m. 173-5°; AcCH₂, p -O₂NC₆H₄, 93.1%, m. 160.5-
70°; AcCHMe, p -O₂NC₆H₄, 90%, m. 130-2°; 2-cyclohex-
anon-1-yl, p -O₂NC₆H₄, 95.1%, m. 182-3°. Refluxing 5 g.
4(5)-phenyl-2-mercaptoimidazole in 80 ml. 38% HCl with
2.75 g. AcCH₂Cl 1 hr. gave after treatment with C and cool-
ing 91.5% 3-methyl-6-phenylimidazo[2,1-b]thiazole HCl salt,
decomp. 228-32°, which with NaHCO₃ gave the free base,
m. 113-13.5°, identical with a specimen prep'd. from 4-
methyl-2-aminothiazole and BzCH₂Br, or from refluxing
4(5)-phenyl-2-acetylmercaptoimidazole 1 hr. in concd.
HCl, or from refluxing the HCl salt of the latter in BuOH 1
hr. The same procedure yielded 2,3-dimethyl-6-phenyl-
imidazo[2,1-b]thiazole, m. 157-8°; HCl salt, m. 237-9°.

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Refluxing 1 g. 4(5)-phenyl-2-mercaptopimidazole in 35 ml. 11% HCl with 1 g. 2-chlorocyclohexanone 0.5 hr. and neutralization with NaHCO₃ gave after decolorization with C 10-phenylimidazo[2,1-b]tetrahydrobenzothiazole, m. 169° (HCl salt, m. 273-4°), which formed in 97% yield on refluxing I in concd. HCl 1 hr., or by heating 2-amino-4,5,6,7-tetrahydrobenzothiazole with BzCH₂Br in EtOH 3 hrs.

G. M. Kosolapoff

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Chem ✓ Imidazolid series. III. Action of α -halo ketones on 2-mercaptimidazoles. P. M. Kochergin and M. N. Sheinkina. J. Gen. Chem. U.S.S.R. 26, 483-5 (1950) (Engl. translation).—See C.A. 50, 13883b. B.M.B.

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KOCHERGIN, P.M.; SHCHUKINA, M.N.

Imidazole series. Part 4: Reaction of sulfuric acid with 2- β -keto-alkyl(aryl)-mercaptoimidazoles. Zhur. ob. khim. 26 no. 6:1723-1727
(MIRA 11:1)
Je '56.

Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut im. S. Ordzhonikidze.
(Imidazole) (Sulfuric acid)

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Imidazole series. IV. Action of sulfuric acid on 2-
mercaptoimidazoles. P. M. Kochergin and
M. N. Shchukina. J. Gen. Chem. U.S.S.R. 26, 1933-7
(1950) English translation). See C.A. 51, 1942c.

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Sulfanilyl derivatives of natural α -amino acids and their analogs. Yuan Cheu-e and M. N. Shechukina (S. Ordzhonikidze All-Union Chem. Pharm. Research Inst., Moscow). *Zhur. Obshchel Khim.* 26, 2872-82 (1956). — The following derivs. of amino acids were found to be relatively weakly antibacterially active at best. To 11.26 g. $H_3NCH_2CO_2H$ in 20 ml. 40% NaOH and 60 ml. H_2O was added 37.5 g. p -

$MeO_2CNHC_6H_4SO_3Cl$ with addn. of NaOH to maintain the alky. of the mixt. over 3 hrs.; after clarification with C and acidification there was obtained p - $MeO_2CNHC_6H_4SO_3NHCH_2CO_2H$, m. 169-70° (from 60% EtOH). Heating 8.15 g. DL- p - $MeO_2CNHC_6H_4SO_3NHCH_2MeCO_2H$ with 8 ml. concd. H_2SO_4 and 40 ml. EtOH 4 hrs. at 80-4° gave 91% Et ester, m. 144-4.5°. Heating 2.58 g. p - $H_3NCH_2SO_3NHCH_2CO_2Et$ with 1.25 ml. 80% $N_2H_4\cdot H_2O$ in 20 ml. abs. EtOH 4 hrs. gave on evapn. 72% p - $H_3NCH_2SO_3NHCH_2CONHNH_2$, m. 160° (from 60% EtOH). Heating DL- p - $H_3NCH_2SO_3NHCH_2MeCO_2H$ with EtOH in the presence of HCl or H_2SO_4 gave 85.3% Et ester, m. 110-11°, which kept 3 days in Et-OH-NH₂ gave 73.5% corresponding amide, m. 170.5-1.5° (from H_2O), which also formed on refluxing the corresponding hydrazide (I) with Raney Ni in 95% EtOH. To 1 g. I in 20 ml. EtOH was added at reflux 1 g. vanillin in 10 ml. EtOH, the mixt. kept 2 days at room temp. and heated 4 hrs. to reflux yielding yellow β - $H_3NCH_2SO_3NHCH_2CONHNH_2CHC_6H_4(OMe)OH-3,4$, m. 172-5°. Treatment of DL-serine in 50% NaOH with p -AcNH₂H₂SO₃Cl gave *N*-(p -acetamidobenzenesulfonyl)-DL-serine (II), m. 211-12° (from

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50% EtOH), which heated with 15% HCl, evapd., and neutralized with NaOAc gave 83.5% *N*-*p*-acetamidobenzene-sulfonyl-DL-serine, m. 212-2.5° (from 50% EtOH), which with EtOH-HCl gave the Et ester, m. 86-7° (HCl salt, m. 176-81°). II (10 g.) and 1.9 g. KOH in 90 ml. H₂O were treated rapidly with 5.05 g. AgNO₃ in 50 ml. H₂O yielding 87.5% Ag salt, which after drying was suspended in C₆H₆ and treated 4.0 hrs. with MeI in the dark yielding, after refluxing 3 hrs., 70% II Me ester, m. 164-6°, which heated gradually with excess SOCl₂ to 0° gave 74% *p*-AcNH₂H₂SO₄NHCH(CH₂Cl)CO₂Me, m. 130-0°, which treated with EtOCS₂K overnight, acidified with HCl, the resulting xanthate deriv. (1.62 g.) taken up in EtOH, treated with 25% NH₄OH, allowed to stand 3 days, acidified with HCl, evapd., heated with 15% HCl until dissolved, then treated with 7.5 g. Zn 0.5 hr., evapd., and neutralized with NaOAc gave 63% *N*-*p*-acetamidobenzene-sulfonyl-DL-cysteine, decomp. 182-92° (from H₂O with addn. of Na₂SO₃); the same formed from DL-cysteine and *p*-AcNH₂H₂SO₄Cl in 10% NaOH after the above treatment. Substitution of EtSNa for EtOCS₂K in the above synthesis gave 38.2% *N*-*p*-aminobenzene-sulfonyl-S-ethyl-DL-cysteine HCl salt, m. 159-02°, when the initially formed intermediate was refluxed with 15% HCl; the same formed from the above cysteine deriv. on treatment with EtI in aq. alc. NaOH. The use of BuSNa gave *N*-*p*-aminobenzene-sulfonyl-S-butyl-DL-cysteine HCl salt, m. 143-52°. To 125 ml. NH₃ was added 2.5 g. L-cysteine followed by 0.96 g. Na and after decolorization of the blue soln. it was treated with 7.6 g. EtI and stirred 3 hrs. After evapn. of NH₃, stirring with H₂O 2 hrs., addn. of alkali to phenolphthalein endpoint, extn. of EtI with Et₂O and treatment of the aq. soln. by *p*-AcNH₂H₂SO₄Cl (III), it gave 38.9% *N*-*p*-acetamidobenzene-sulfonyl-S-ethyl-L-cysteine, m. 180-2° (from 60% EtOH).

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[α]D -8° ; this heated 1.5 hrs. with 15% HCl gave the *p*-amino analog, m. 182-3°, [α]D -12.8° . III and DL-glutamic acid in aq. NaOH gave, after hydrolysis of the Ac group with 15% HCl, 50.5% *N*-*p*-aminobenzenesulfonyl-DL-glutamic acid, m. 175-5.5°. To 13.05 g. 2-bromohexanoic acid in 45 ml. EtOH was added 21.1 g. *p*-H₂N₂C₆H₄SO₃NH₂ and heated 8 hrs. on a steam bath yielding after sepn. of KBr, extn. with 10% Na₂CO₃, and acidification with AcOH 78% *N*-*p*-aminobenzenesulfonyl-DL-norleucine, m. 164°, HCl salt, m. 172-6°. Reaction of III with 6-aminohexanoic acid in aq. NaOH gave 72% *N*-*p*-acetamidobenzenesulfonyl-leucine, m. 146-7°; this gave the *p*-amino analog, m. 134°; Et ester, m. 94°. Similarly were prep'd.: *p*-AcNH₂C₆H₄SO₃NHCH(CO₂H)CH₂Fh, m. 231°; its *p*-amino analog Et ester, m. 120-1°, and its hydrazide, m. 192-3°; *p*-AcNH₂C₆H₄SO₃NHCH(CMe₂SH)CO₂H, m. 234-9°, and its *p*-amino analog, m. 184-8°; *p*-AcNH₂C₆H₄SO₃NHCH(CH₂CH₂SM₂)CO₂H, m. 149-51°, and its *p*-amino analog, m. 159-03°; *p*-H₂N₂C₆H₄SO₃NHCH(CH₂CH₂SM₂)CO₂Et, m. 105-6°; its hydrazide; *N*-*p*-acetamidobenzenesulfonyltryptophane, m. 238-9°; its *p*-amino analog, m. 188-90°. *N*-*p*-Acetamidobenzenesulfonylproline, m. 228-9°; its *p*-amino analog m. 126-8°, and the Et ester of the latter m. 145-7°. Addn. of 17.2 g. iso-BuCHO to 11 g. 95% NaCN, 14 g. NH₄Cl, and 50 ml. H₂O with good stirring over 40 min., heating 1.5 hrs. at 60-3°, sepn. of the aminonitrile by extn. with Et₂O, and heating this with concd. HCl 10 hrs. gave on evapn. crude product which after cryst. from a little hot

H₂O gave 8.6 g. DL-leucine-HCl, which with NaHCO₃ gave 30.5% DL-leucine, m. 288-70°. G. M. Kosolapoff

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a ✓ Synthesis of β -(*N*-2-chlorophenoxyethyl)propionic acid, its derivatives and derivatives of β -*N*-phenothiazylpropionic acid. N. V. Savitskaya, Yu. S. Tsizin, and M. N. Shchukina (S. Ordzhonikidze All-Union Chem. Pharm. Research Inst., Moscow). *Zhur. Obschei Khim.* 26, 2900-5 (1956).

— Heating 17.4 g. 3-chlorodiphenylamine, 5.8 g. S, and 0.2 g. iodine 1.3 hrs. at 160–80°, until H₂S evolution stopped gave 60.5% 2-chlorophenothiazine, m. 199–200.5° (from MePh). *b*

This (10 g.) and 30 ml. CH₃:CHCN and 0.1 g. hydroquinone treated at room temp. with 2 ml. PhNMe₂:OH soln. (from 0.76 g. toluenesulfonate salt) and heated 1.5 hrs. at 80°, gave 81% β -(*N*-2-chlorophenoxyethyl)propionitrile (I), m.

188–9° (from AcOH), which heated in sealed ampul with concd. H₂SO₄:EtOH 6 hrs. at 130–40°, then refluxed with 26% KOH 6 hrs. and acidified, gave 87% β -(*N*-2-chlorophenoxyethyl)propionic acid (II), m. 166.5–58° (from MeOH); if the treatment with KOH is omitted there is formed the Et ester (III), b.p. 205–0°, m. 64.5–66° (from petr. ether). *c*

Hydrogenation of I over Raney Ni in EtOH under 10 atm. NH₃ at 100–10° and 30 atm. H₂ gave *N*-(3-amino-propyl)-2-chlorophenothiazine; HCl salt, m. 233–5° (from dry EtOH). III and satd. NH₃ in dry EtOH gave in 24 hrs. β -(*N*-2-chlorophenoxyethyl)propionamide, m.

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143.5-5.5° (from C₆H₆); similarly III and 65% N.H₄.H₂O in EtOH heated 23 hrs. on steam bath gave the corresponding hydrazide, m. 132.5-3.5° (from MeOH); *p*-acetamidobenzylidene deriv., m. 236-7°. II and PCl₅ in C₆H₆ gave the crude acetyl chloride which was freed of solvent and POCl₃ by mild heating *in vacuo* and washing with C₆H₆, and this solid chloride was refluxed with HOCH₂CH₂Cl 11 hrs. yielding 70% II 2-chloroethyl ester, m. 83-4° (from EtOAc), which heated with Me₂NNH₂ 5.5 hrs. at 100° in ampul gave 40% 1,1-dimethyl-1-[2'-(*β*-N-2-chlorophenylazyl)propionyloxyethyl]hydrazoneum chloride, m. 181-5° (from EtOAc-EtOH). Heating *β*-N-phenoxyacrylic acid with MeOH in the presence of H₂SO₄ 0 hrs. gave its Me ester, 83%, m. 64.5-5.5°, b.₁ 210-14°; Et ester, prep'd. similarly to above from the corresponding nitrile in 84% yield, m. 63.5°, b.₁ 195-202°. The free acid treatd with PCl₅ as above, followed by NH₃, gave *β*-N-phenoxyacetylpropionamide, m. 125-6° (25%) (from aq. EtOH). The Et ester and N₂H₄.H₂O heated 23 hrs. gave the hydrazide, decamp. 98-9°, whose *p*-acetamidobenzylidene deriv., m. 192-3°, and 4-hydroxy-3-methoxybenzylidene deriv., m. 200.5-202° (from AcOH). Treatment of the acyl chloride, prep'd. as above, with Me₂NCH₂CH₂OH in C₆H₆ gave *β*-N-phenoxyacetylpropionic acid dimethylaminooethyl ester, 66%, b. 214-16°; HCl salt, m. 141.5-2.5° (from PhCl). Similarly the acyl chloride and ClCH₂CH₂OH gave the 2-chloroethyl ester, m. 75-6°, which with Me₂NNH₂ kept 2 days at room temp. and 3 days at 0° gave 1,1-dimethyl-1-[2'-(*β*-N-phenoxyazyl)propionyloxyethyl]hydrazoneum chloride, m. 174.5-5.5° (from abs. EtOH).

G. M. Kosolapoff

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SLUCHUKINA, M. N.

Imidazole series. VI. Action of bromoacetaldehyde and its derivatives on some 2-mercaptopimidazoles. P. M. Kochergin and M. N. Sluchukina (S. Ordzhonikidze All-Union Chem. Pharm. Research Inst., Moscow). *Zhur. Obshch. Khim.* 26, 2045-10 (1956); *cf. C.A.* 51, 5050b. — On the basis of structures of intermediates described below, the mechanism for closure of imidazo[2,1-*b*]thiazole rings appears to proceed by formation of 2-oxalkylimidazolyl sulfides, which cyclize at the carbonyl group and the NH group of the imidazole portion, yielding 3-hydroxyimidazo[2,1-*b*]thiazolines, which then lose H₂O yielding the final product. The structures of the products described below are confirmed by infrared spectra which are reproduced. To 1.3 g. Na dissolved in 80 ml. abs. EtOH was added 10 g. 4(5)-phenyl-2-mercaptopimidazole (I), followed by 11.3 g. BrCH₂CH(OEt)₂, and the mixt. refluxed 11 hrs., filtered from NaBr, washed with H₂O and evapd. yielding 98.2% 1(5)-phenylimidazo[2-yl]mercaptoacetaldchyde di-Et acetal, a viscous oil, whose picrate, m. 120-7°; the analogous di-Me acetal, an oil, was prep'd. similarly. The di-Et acetal (II) (8.9 g.) was refluxed 1.5 hrs. with 20 ml. POCl₃, freed of excess POCl₃ *in vacuo*, treated with H₂O and neutralized with NaHCO₃, and extd. with CHCl₃, yielding 75.1% 3-ethoxy-5-phenylimidazo[2,1-*b*]thiazoline, m. 122° (from EtOHD (picrate, decomp. 197-8°); similarly the di-Me acetal gave the 3-methoxy analog, an oil, whose HCl salt, decomp. 141-2°, and

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treatment with NaHCO₃ gave the pure free base, m. 71.5-2.5°; picrate, decomp. 172-3°. Refluxing 8.7 g. EtOCHBr-CH₂Br in 70 ml. H₂O until a soln. formed, followed by addn. of 6.6 g. I and refluxing 1 hr., neutralization with NaHCO₃, and filtration gave 8 g. 3-hydroxy-6-phenylimidazo[2,1-b]thiazoline, decomp. 160-1° (HCl salt, decomp. 163-5°; picrate, decomp. 145-6°, forms a dihydrate). The same components react similarly in refluxing C₆H₆; the same products also formed in 88% yield on refluxing II with 38% HCl 1.3 hrs. or on standing 1 day in aq. HCl. Refluxing 6 g. 4(6)-p-nitrophenyl-2-mercaptopirimidazole with 6.3 g. EtOCHBr-CH₂Br in H₂O 3 hrs. gave after neutralization 98.5% 3-hydroxy-6-p-nitrophenylimidazo[2,1-b]thiazoline (IIa), decomp. 203-4° (from Me₂CO). Refluxing 2 g. 2-amino-thiazole with 3.97 g. BzCH₂Br in 45 ml. EtOH 1.5 hrs., evap., and treating with Et₂O gave 90.0% 6-phenylimidazo[2,1-b]thiazole HBr salt, m. 114-16°, which with NaHCO₃ gave the free base (III), m. 148-6.5° (from aq. EtOH); HCl salt, m. 153-4°; sulfate, m. 210-11° (monohydrate, from EtOH); picrate, m. 223-3.5°. II (1.4 g.) in 6.6 ml. 95% H₂SO₄ heated to 50° over 0.5 hr., then poured into 12-15 ml. H₂O and heated on a steam bath 1 hr., neutralized with NaHCO₃, and extd. with CHCl₃, yielded the above product, isolated as picrate, m. 223°, in 0.15-g. yield. III formed in 74.1% yield on heating 1 g. 3-hydroxy-6-phenylimidazo[2,1-b]thiazoline with 6 ml. 95% H₂SO₄ 7-10 min. at 30° and keeping several hrs. at room temp.; the yield was 67.8% if POCl₃ was substituted for H₂SO₄, and the mixt. refluxed 10 min. Similarly, up to 92% yields were obtained on heating the 3-MeO or 3-EtO derivs. of phenylimidazo-thiazoline with 95% H₂SO₄ as above. IIa (3 g.) refluxed 2 hrs. with 50 ml. POCl₃ gave after aq. treatment and addn.

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of Na₂CO₃, 96.4% 2-p-nitrophenylimidazo[1,5-b]thiazole, m. 238-4° (from AcOH). Heating 3.5 m. 95.6% H₂SO₄ with 0.3 g. 3-methoxy-8-phenylimidazo[2,1-b]thiazoline-HCl salt 0.5 hr. on a steam bath, cooling, and dilg. with 20 ml. ice H₂O, gave 79.7% 8-p-sulfophenylimidazo[2,1-b]thiazole (IV), spindly crystals (from H₂O), does not m. 380°; monohydrate loses H₂O at 100°; the 3-HO analog gave the same product in 77% yield, as did the 3-HO analog in 84.8% yield (in this case a small amount of relatively insoluble III also formed). Heating III with 95% H₂SO₄ 0.5 hr. at 100° gave 64.1% IV. VII. Action of acetic anhydride on 2-β-oxoalkyl(aryl)mercaptoimidazoles. P. M. Kochergin. *Ibid.* 2014-21. Refluxing 1.25 g. 4(5)-phenyl-2-acetylmercaptoimidazole with 6 ml. Ac₂O 5-7 min., cooling, and filtering, gave 1.21 g. 1-acetyl-5-phenyl-2-acetylmercaptoimidazole, m. 158-9°, with total yield of 90% being obtained after concn. of the mother liquors. Similarly, from corresponding imidazoles were prep'd. the following 1-acetyl-5-phenyl(or p-nitrophenyl)-2-β-oxoalkyl(aryl)mercaptoimidazoles: 5-phenyl-2-(1-methyl-2-oxotropyl), 99.7%, m. 152-4°; 5-phenyl-2-acetophenonyl, 94.6%, m. 171-1.6°; 5-phenyl-2-(m-nitroacetophenonyl), m. 161-2°; 5-phenyl-2-(2-cyclohexenonyl), 78.1%, m. 158-7°; 5-p-nitrophenyl-2-acetonyl, 95.7%, m. 182-3°. Heating 0.7 g. 4(5)-phenyl-2-p-nitrophenacylmercaptoimidazole with 15 ml. Ac₂O 8-10 min. at 100°, removing Ac₂O *in vacuo*, and cooling gave 76% 1-acetyl-5-phenyl-2-p-nitrophenylmercaptoimidazole, m. 169-70° (from EtOH); if the reaction mixt. is refluxed, the same product forms along with 2-p-nitrobenzyl-3-methyl-5-phenylimidazo-

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[2,1-b]thiazole, m. 190°, isolated by treating the mother liquors with alc. HCl. Refluxing 0.8 g. 1-acetyl-5-phenyl-2-acetonylmercaptoimidazole with 0.8 g. NaOAc and 4.5 ml. Ac₂O 0.8 hr. gave 98.6% 2-acetyl-5-phenylimidazo[2,1-b]thiazole, m. 150-1° (from EtOH). Similarly was prepd. 3-methylimidazo[2,1-b]thiazyl-2-benzoyl analog, m. 227-8°, and 2-acetyl-3-methylimidazo[2,1-b]thiazoly-5-p-nitrophenyl analog, m. 186-7°, as well as 3-m-nitrobenzoyl-3-methyl-5-phenylimidazo[2,1-b]thiazole, m. 144-5°, and its 2-p-nitrobenzoyl analog, m. 180°. Refluxing 5 g. 4(5)-phenyl-2-mercaptopimidazole in 75 ml. BuOH with 3.85 g. 3-chloro-2,4-pentanedione 15 min., followed by evapn. in vacuo, gave 99.2% 4(5)-phenyl-2-(α -acetoacetyl)-mercaptoimidazole, m. 135-6° (HCl salt (I), decomp. 148-51°). To 0.56 g. Na in 75 ml. BuOH was added 5.4 g. 4(5)-p-nitrophenyl-2-mercaptopimidazole and 3.4 g. 3-chloro-2,4-pentanedione and the mixt. refluxed 1 hr. gave 91% 4(5)-p-nitrophenyl-2-(α -acetylacetonyl)mercaptoimidazole (II), m. 144-5° (from BuOAc). I (2 g.) refluxed 1 hr. in 10 ml. BuOH gave on cooling 74.5% 2-acetyl-5-methyl-5-phenylimidazo[2,1-b]thiazole, m. 203-3.6°, isolated as HCl salt, m. 232-4°. Refluxing 2.7 g. II in 40 ml. POCl₃ 0.5 hr.

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followed by removal of POCl_3 *in vacuo* and treatment with aq. NaHCO_3 gave 98% 2-acetyl-3-methyl-6-p-nitrophenylimidazol[2,1-b]thiazole, m. 281-1.5° (from AcOEt); this formed in 87% yield from 4-methyl-5-acetyl-2-aminothiazole and $\text{BrCH}_2\text{COC}_6\text{H}_4\text{NO}_2\text{p}$, after refluxing 2 hrs. in EtOH , and 1 hr. with AcOH after removal of EtOH . — G. M. K.

Cyclization of thioburets⁷ to substituted 1,2,4-thiadiazoles.⁷ F. Kurzer (Roy. Free Hosp. School Med., London). *Chem. & Ind. (London)* 1956, 1482.—Dealkylation of Ph-NHCSNHC(OR):NH (I) gave PhNHCSNHCONH₂ (II), m. 158-60°; dehydrogenation of I or II with Br or H_2O_2 gave good yields of S.N:C(OR).N:CNHPh (III). R and w.p.

were given for I: Me, 129-80°; Et, 98-9°. For III: Me, 158-9°; Et, 167-8°; H, 212-13°. — G. R. Yone

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Transformations of *o*- and *p*-nitrotoluene in alkaline medium. M. N. Shchukina and G. S. Prudovoditseva
(S. Ordzhonikidze All-Union Chem. Pharm. Sci. Res. Inst., Moscow). Doklady Akad. Nauk S.S.R. 110,
230-3 (1956); cf. Ger. 86,874; Plzov. C.A. 44, 1108.

While basic treatment of *o*-MeC₆H₄NO₂ (I) results in reactions probably proceeding through intermediates of an anthranil type, the *p*-isomer must form similar polymeric intermediates. I in NaOH with S should yield *o*-H₂NC₆H₄CHO. The reaction yields 14% of this aldehyde and some *o*-MeC₆H₄NH₂. If the soln. of S in NaOH is added to the mixt. only after I had been refluxed with 20% aq. alc. NaOH for several hrs., there is obtained 15% 2-indazylbenzyl alc. Anthranil with S and NaOH gave anthranilic acid and *o*-H₂NC₆H₄CHO; phenyl-*N*-phenylnitrone gave PhCH=NPh, while *p*-nitrophenyl-*N*-*p*-tolylnitrone gave *p*-MeC₆H₄NH₂ and an anhydropolymer of *p*-H₂NC₆H₄CHO. The red substance formed from *p*-MeC₆H₄NO₂ and NaOH is chemically inert to acids, bases, and oxidation-reduction reagents; its spectrum (infrared) does not have the bands typical of N=O group of nitrones (butyl-*N*-methylnitronate and *N*-oxides of pyridine and Me₂N show intense bands at 1185-1250 cm.⁻¹ and 920-950 cm.⁻¹); hence the groups which connect the polymer links are not nitrone groups but probably amide links. This is confirmed by the fact that *p*-nitrophenyl-*N*-*p*-tolylnitrone treated with aq. alc. NaOH gave a very inert polymer, which with piperidine gave *p*-nitrobenzo-*p*-toluidide, which indicates that the initially formed nitrone undergoes under the action of alkali, a rearrangement of the Beckmann type, forming a *p*-linked polyamide. I with NaOH may be represented by formation of unstable lactam from the initially formed anthranil; the latter gives rise to a variety of products depending on the subsequent treatment.

G. M. Kosolapoff

Signature of Dr. R.

Transformations of *o*- and *p*-nitrotoluenes in alkaline medium. M. N. Shchukina and G. S. Predvoditeleva.
Proc. Acad. Sci. U.S.S.R., Sect. Chem. 110, 585-8 (1956)
(English translation).—See *C.A.* 51, 49908. B. M. R.

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EM

SHCHUKINA, M. N.

3-Dimethylaminopropanol M. N. Shchukina, N. V.
Savitskaya, T. V. Gortinskaya, Yu. S. Tsitin, and V. G.
Samolovova. U.S.S.R. 105,447, May 25, 1957. The
compd. is obtained by reduction of ethylene cyanohydrin and
methylation of the resulting 3-amino propanol. The reduc-
tion of ethylene cyanohydrin is carried out in a ammoniacal
alc. soln. and the methylation is done with CH_3O in HCO_2H .
M. Hosen

6
1-4E3d
1-4E4f

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702

SCHUKINA, MN.

Distr: 4E4

2,5-Di(4-pyridyl)-1-amino-1,3,4-triazole and its derivatives. V. G. Yasunskii, L. N. Pavlov, V. G. Ermolalova, and M. N. Schukina. *Khim. Nauka i Prom.* 2, 658 (1957). In the condensation of isonicotinoyl acid with hydrazine product was found which is probably 2,5-di(4-pyridyl)-1-amino-1,3,4-triazole (I), stable in boiling HCl. KMnO₄ and concd. HNO₃ reacted with I to give 2,5-di(4-pyridyl)-1,3,4-triazaide (II), m. 286-8°. Its dil-HCl salt (m. 300-2°) and its dipicrate (m. 257-9°) were prep'd. Boiling I with PhCHO at 180-8° gave the benzaldazine derivs. of II (m. 197-200°) and of 2,4-di(4-pyridyl)triazole, m. 286-0°. I. Bencowitz

SHCHUKINA, M. N.

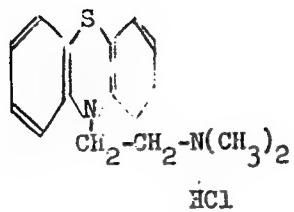
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"Complexon-IV" and its analogs. V. G. Vashunskii and M. N. Shchukina. Khim. Nauka i Prom. 2, 662-3 (1987). *cis*- (I) and *trans*- (II) -1,2-Diaminocyclohexane were prep'd. The expected reaction of I with $\text{ClCH}_2\text{CO}_2\text{H}$ (cf. Schwartzenbach, et al., C.A. 44, 548c) did not take place. On the other hand II reacted, giving, *1,2-diamino-cyclohexane-N,N,N',N'-tetracetic acid* (III), the properties of which were identical with those of "complexon-IV" which S. believed was the *cis* isomer. The *trans*-1,2-diaminocyclopentane-*N,N,N',N'*-tetracetic acid (IV) and the corresponding butane analog (V) were prep'd. by condensation of the respective diamine with $\text{ClCH}_2\text{CO}_2\text{H}$. The values of pK_1 , pK_2 , pK_3 , and the stability consts. of the complex CaX^+ of IV were 2.4, 3.3, 7.56, 10.80, and 12.2; and of V 2.7, 2.8, 5.80, 9.75, and 8.0. The corresponding values of ethylenediamine-*N,N,N',N'*-tetracetic acid (given for comparison) were 1.998, 2.072, 6.161, 10.26, and 10.59. V was the least stable. It was concluded that the essential factor for increased stability of the internal complex of metalocycles was that the amino groups be close to each other and that their free rotation about the C1-C-2 bond be hindered.
1. Bencowitz

122. Synthesis of Aminazine and Other Phenothiazine Derivatives

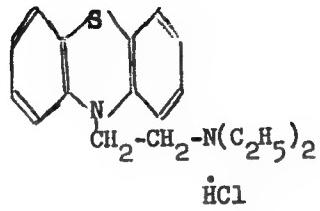
"On the Synthesis of Aminazine and Its Analogues," by N. M. Shchukina, N. V. Savitskaya, and Yu. S. Tsizin, All-Union Scientific-Research Chemicopharmaceutical Institute imeni S. Ordzhonikidze, Meditinskaya Promyshlennost' SSSR, Vol 11, No 3, Mar 57, pp 20-24

This article describes a method of synthesizing aminazine and its analogues--etizine, dinezine, diprozine, and mul'tezine -- all phenothiazine derivatives. All have been found to possess important pharmacological properties, i.e., they act as spasmolytics and sedatives, affect the

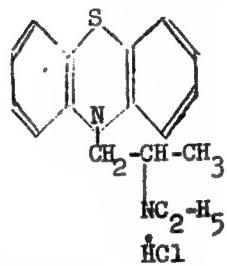
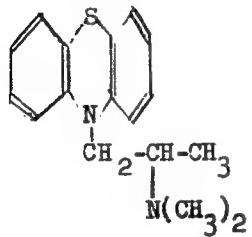
central nervous system, and are used as therapeutic agents in nervous diseases and in the practice of psychiatry. Aminazine is the only one of the group of phenothiazine derivatives in which there is substitution in the nucleus. In all other cases, only the nitrogen is replaced by N-alkylaminoalkyl radicals. They are easily synthesized by the heating of phenothiazine with haloidoalkyl-aminoalkyl compounds and alkaline reagents. The best results are obtained when condensation is carried out with sodium hydroxide, with the water and immiscible solvents -- benzene and toluol -- being continuously drained off, a method developed at the experimental plant of the All-Union Scientific-Research Chemicopharmaceutical Institute by L. I. Morozovskaya and M. A. Vorob'yev. N-dialkylaminoalkylphenothiazines are obtained having the following structural formulas:



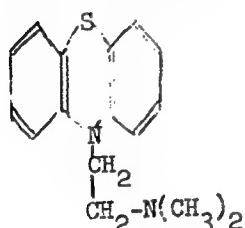
Etizine (anergan)



Dinezine (diparkol)



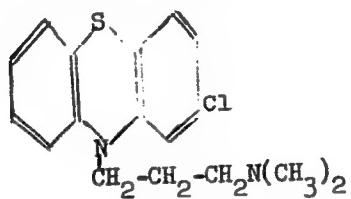
Diprozine (fenergan)



HCl

Promazine

Parfezine (parsidol)



HCl

Aminazine (largactile,
Chlorpromazine)

Other ways of compounding the dialkylaminoalkyl radical with phenothiazine by a method of condensing phenothiazine with substances having an active unsaturated system or with substances with an oxide radical are described. (u)

GORTINSKAYA, T.V.; SAVITSKAYA, N.V.; SAMOLOVOVA, V.G.; TSIZIN, Yu.S.;
SHCHUKINA, M.N.

Obtaining dimethylaminopropanol from ethylene cyanohydrin. Med.
prom. 11 no.4:23-25 Ap '57. (MIRA 10:6)

i. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imeni S. Ordzhonikidze.
(PROPANOL) (HYDRACRYLONITRILE)

SHCHUKINA, M.N.; GOLOMBIK, E.S. [deceased]

Producing phenylacetamide. Med.prom. 11 no.7:42-44 J1 '57. (MLRA 10:8)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imeni S.Ordzhonikidze
(ACETANILIDE)

YASHUNSKIY, V.G.; PAVLOV, L.N.; YERMOLAYEVA, V.G.; SHCHUKINA, M.N.

By-product of the condensation of isonicotinic acid and hydrazine
hydrate. Med.prom. 11 no.12:38-40 D '57. (MIRA 11:2)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze.
(ISONICOTINIC ACID) (HYDRAZINE) (TRIAZOLE)

SHUKINA, M.N. (Moskva); YUAN' CHEN-YE [Yuan Cheng-i] (Shankhay).

Mercapto acids and mercaptocarboxylic acids. Usp. khim. 26 no.5:
608-624 My '57.

(MLRA 10:6)

(Mercapto compounds)

SUCHUKINA, N.N.

✓ Mercapto-analogs of lysine and some of their derivatives
 1. Synthesis of ϵ -mercaptop- ϵ -aminocaproic acid and its *S*-alkyl and *N*-sulfanilyl derivatives. Chen-B Yuan and M. N. Shchukina (S. Ordzhonikidze All-Union Chem. Research Inst., Moscow). Zhur. Obshchel. Khim. 27, 294-311 (1957).—Heating 74 g. $\text{EtO}_2\text{C}(\text{CH}_2)_4\text{CH}_2$, 66 g. $\text{CS}(\text{NH}_2)_2$, and 315 ml. 45% HBr 10 hrs. on a steam bath, followed by addn. of 644 ml. 20% NaOH with cooling and refluxing under N 3 hrs., heating 1 hr. at 120° in an N stream, cooling, acidifying and extg. with Et_2O gave 3.1 g. $\text{HO}_2\text{C}(\text{CH}_2)_4\text{SH}$ (I), b_{14} 112-16°, and its *disulfide*, 0.9 g., b_{14} 163-70°, m. 80-2°. Heating 16.5 g. KSH in 200 ml. EtOH with 33.45 g. $\text{EtO}_2\text{C}(\text{CH}_2)_4\text{Br}$ 2 hrs. gave 64.5% $\text{EtO}_2\text{C}(\text{CH}_2)_4\text{SH}$, b_{14} 81-5°, n_D^{20} 1.4503, d_2^{20} 0.9895; Pd salt, yellow solid. The ester formed from the acid and EtOH-EtCl, in 65% yield. The ester (14.08 g.) heated with 1.84 g. Na in 60 ml. EtOH and 13.75 g. EtI 1 hr. at 60-70°, then refluxed 3 hrs. gave after filtration, concn., treatment with Na_2CO_3 and extn. with Et_2O , 14.9 g. crude or 11.8 g. pure $\text{EtS}(\text{CH}_2)_4\text{CO}_2\text{Et}$ (II), b_{14} 130-4°, b_{14} 150°, n_D^{20} 1.4620, d_2^{20} 0.9675; similarly was prep'd. 75% *S*-benzyl analog (III), b_{14} 172-3°, 1.6223, 1.0452 which loses the PhCl group in liquid NH₃ under action of Na yielding I. II (0.5 g.) with 2.9 g. 27.8% H_2O_2 in 26 ml. AcOH in 3 days, gave 50.5% $\text{EtSO}(\text{CH}_2)_4\text{CO}_2\text{Et}$, b_{14} 119-200°; similarly was prep'd. the *S*-benzyl analog, m. 58-7°. II (3.1 g.) in 0.346 g. Na and 15 ml. dry EtOH was treated with 65 ml. H₂O and refluxed 13 hrs. yielding on evap. 70.8% *EtS*($\text{CH}_2)_4\text{CO}_2\text{Na}$, does not m. 300°; the Na salt of the *S*-benzyl analog, was prep'd. similarly. III (3.3 g.) and an unstated amt. of (CO_2Et)₂ added to EtONa from 30 ml. EtOH and 1.15 g. Na, heated at 50-60°/100 mm. Hg 2 hrs., dild. with H₂O, acidified with H_2SO_4 , and extd. with Et_2O , gave 65% $\text{PhCH}_2\text{S}(\text{Li}^+)_2\text{CH}(\text{CO}_2\text{Et})_2$ (IV), b_{14} 130-6°.

Yuan Chen & Shchukina, M. N.

this kept with EtOH satd. with NH₃ 1 day gave the monoamide, m. 96-8° (from EtOH), IV (13.35 g.) in 0.21 g. Na and 18 ml. dry EtOH treated at 2° with 4.5 g. BuONO and stirred 2.5 hrs. at room temp. gave after evapn., diln. with H₂O, and extnd. with Et₂O 90% oily oxime deriv. which (6.02 g.) in 15 ml. AcOH and 15 ml. Ag₂O treated slowly with 5 g. Zn dust activated with HCl and stirred 2 hrs., filtered and concd. gave 72% PhCH₂S(CH₂)₂CH₂(CO₂Et)NHAc, m. 125-7° (from EtOH-Et₂O), which heated at 100° 18 hrs. with 15% HCl, washed with Et₂O, evapd. several times to remove excess HCl, clarified with C and treated in aq. soln. with 3 ml. pyridine gave 78% PhCH₂S(CH₂)₂CH(NH₂)CO₂H (V), decomp. 238-12° (from EtOH-Et₂O). This (1.45 g.) in 90 ml. liquid NH₃ treated with 0.204 g. Na and stirred 3 hrs. at room temp., then diln. with H₂O, acidified with HCl, extd. with Et₂O, and the org. layer evapd. and extd. with alc. HCl gave on evapn. of the ext. 0.75 g. HS(CH₂)₂CH(NH₂)CO₂H·HCl salt, m. 228-34°. This with *p*-AcNHCO₂H₂SO₃Cl and Na₂S₂O₈ gave the oily acetyl/sulfanilyl deriv. which heated 1 hr. with 15% HCl at 100° gave 81% HS(CH₂)₂CH(NHO₂SC₆H₄-p-C₆H₄)CO₂H·HCl salt (VI), decomp. 203-8° (from 10% HCl). V treated as above with Na in liquid NH₃ gave on treatment with Bu₂N⁺ 70.5% Bu₂S(CH₂)₂CH(NH₂)CO₂H, decomp. 230-2° (from H₂O). This with *p*-AcNHCO₂H₂SO₃Cl in 0.5N NaOH followed by heating with 15% HCl 1 hr. gave a product, m. 35-43%; after treatment with 10% HCl it gave 70% Bu₂S(CH₂)₂CH(NHO₂SC₆H₄-p-C₆H₄)CO₂H·HCl salt, m. 235-43° (from 10% HCl); the same product form VI by shaking VI with Bu₂N⁺ in aq. alc. NaOH.

G. M. Kosolapov

R MV

Shechukina, M. N.

Mercapto analogs of lysine and some of their derivatives.

II. Synthesis of α -mercaptop- ω -amino- and α , α -dmercaptop-

caproic acids and their S-alkyl and N-sulfanilyl derivatives.

Chen-B Yuan and M. N. Shechukina (S. Ordzhonikidze All-

Union Chem. Pharm. Sci. Research Inst., Moscow).

Zhur. Obshchel Khim. 27, 1163-8 (1957); cf. C.A. 51, 16291e.

—Heating 1.6 g. KSH and 3.14 g. $BzNHCH_2(CH_2)_4CH_2BrCO_2H$ in EtOH 1 hr. gave a ppt. which after extn. with EtOH and concn. of the ext. gave an oil which after reppn. from Na_2CO_3 with HCl gave $BzNH(CH_2)_4CH(SH)CO_2H$, m.

152-7° (50% EtOH); hydrolysis with 20% HCl 18 hrs. and treatment of the crude product with $Pb(OAc)_4$ gave a cryst. Pb mercaptide which decompr. with H_2S yielded 41.5% $H_2N(CH_2)_4CH(SH)CO_2H \cdot HCl$ (I) after evapn. from aq. HCl; the pure salt, decomp. 122-4.5° (EtOH-Et₂O). This treated with dry HCl in abs. EtOH 2 days gave the Ester, b.p. 182-4°, which is sol. in aq. NaOH, but the solns. slowly ppt. the disulfide oxidation product. I in EtOH-2N NaOH treated with BuLi in N at room temp. 15 hrs. gave 82.3% $H_2N(CH_2)_4CH(SBu)_2CO_2H$, isolated as HCl salt (II), m. 223-30°. Heating p -AcNH₂H₂SO₄NH(CH₂)₄CH₂CO₂H in CHCl₃ with SOCl₂ 0.5 hr., followed by treatment with Br in CHCl₃ at 50°, and finally at 90° 1.5 hrs. gave, after ice treatment, an unstated yield of p -AcNH₂H₂SO₄NH(CH₂)₄CHBrCO₂H, decomp. 125-8° (aq. EtOH). This with alc. KSH, as above, gave the expected mercapto deriv., which in crude state was refluxed 1 hr. with 15% HCl, yielding 50.5% p -H₂NCH₂SO₄NH(CH₂)₄CH(SH)CO₂H.HCl (III), decomp. 182-7°; this also formed in 37.8% yield on treatment of 1.2 g. I with 0.2 g. Na hydrosulfite and 1.4 g. p -AcNH₂H₂SO₄Cl. The latter reacted with

YUAN, CHEN-F., SHUCHIKI AND, PI. N.

II in *N* NaOH to yield after hydrolysis with HCl 78.5% *p*-
 $H_3NC_6H_4SO_3NH(CH_2)_2CH(SBu)CO_2Et$, *m.* 171.5-2.5°
(10% HCl), which also formed from III and BuI in *N* NaOH in EtOH, the yield being 46.2%. Refluxing 15.3 g.
KSH with 16 g. Br(CH₂)₂CHBrCO₂Et in EtOH 18 hrs. gave
25% HS(CH₂)₂CH(SH)CO₂Et, (IV) *b*_{1,1} 100-2°, *d*₂₀ 0.9865,

*n*_D²⁰ 1.4452, and 41.7% S.S.(CH₂)₄.CHCO₂Et, *b*_{1,1} 187.5-9°.
Refluxing IV with EtI in EtOH 12 hrs. gave E.S(CH₂)₄CH-
(SEt)CO₂Et, 81.1%, *b*_{1,1} 134-6°, *d*₂₀ 0.9889, *n*_D²⁰ 1.4753.

G. M. Kosolapoff

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PM

Shechukina, M. N.

✓ Synthesis of mercapto amine compounds. I. Synthesis of 11-amino-10-hydroxyundecanoic acid and related compounds. Yu. V. Markova, K. K. Kuzmina, and M. N. Shechukina (S. Ordzhonikidze All Union Chem. Pharm. Sci. Research Inst., Moscow). *Zhur. Obshchey Khim.* 27, 1270-3 (1957).—Oxidation of 24.8 g. Me 10-undecenoate in CHCl₃ with BzO₂H overnight at 0° gave 67.9% Me 10,11-epoxyundecanoate (I), m.p. 168-74°. Similarly, 1-benzoyl-1-decene gave 76.7% corresponding oxide, m. 37°, b.p. 225-31°. This with Et₂O-HCl in 2 hrs. gave 1-chloro-2-hydroxy-10-benzoyledecane, m. 62-4°. Similarly, I gave 100% Me 11-chloro-10-hydroxyundecanoate, b.p. 200-2°, m. 38-41°, whose free acid in 1 day in 25% NH₄OH gave 90% 11-amino-10-hydroxyundecanoic acid, m. 199-200°; HCl salt, m. 127-8°; HBr salt, m. 119-21°. Heating 1-benzoyl-1-decene oxide with 33% NH₄OH in an ampul 8 hrs. at 150° gave a little bis(10-benzoyl-3-hydroxydecyl)amine, m. 116-18°. Heating 1-chloro-2-hydroxy-10-benzoyledecane with 33% NH₄OH as above gave a low yield of the above secondary amine; but similar reaction with 18% alc. MeNH₂ gave a little 1-methylamino-3-hydroxy-10-benzoyledecane, m. 78-80.5°. II. Synthesis of 11-amino-10-mercaptoundecanoic acid and related compounds. *Ibid.* 1274-6.—Heating 11-amino-10-hydroxyundecanoic acid HCl salt (10 g.) and 30 ml. SOCl₂, finally at 50-60°, gave 86% 11-amino-10-chloroundecanoyl chloride HCl salt, decomp. 117.5-19.5°, which refluxed in abs. EtOH 8 hrs. gave 03% Et 11-amino-10-chloroundecanoate HCl salt, m. 133-5° (EtOH). This (2 g.) in 15 ml. H₂O

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MAKKOVA, H. V., KUZMINA, K. K. and
was treated with 0.5 g. CS₂ and 2.5 ml. 22% NaOH, yielding
75% 2-mercapto-5-(8-carboxyacetyl)thiazoline (II), m. 55.5-
7.5° (aq. EtOH). Similarly was prep'd. the 8-carboxyacetyl
analog, m. 139-41°, which required merely the use of a
larger amt. of 22% NaOH. I (3 g.) and 50 ml. concd. HCl
in a sealed tube 5 hrs. at 150° gave 50%, 11-amino-10-mer-
captoundecanoic acid HCl salt, m. 139-42° (EtOH). Shaking
2.14 g. Me 10-undecenoate oxide with 1.64 g. HSCH₂-
CH₂NH₂ in H₂O 50 hrs. gave 10% MeO₂C(CH₂)₄CH(OH)-
CH₂SCH₂CH₂NHCH₂CH(OH)(CH₂)₂CO₂Me, m. 68-73°.
Similar reaction using 10-benzoyl-1-decene oxide gave a low
yield of B-(CH₂)₄CH(OH)CH₂SCH₂CH₂NHCH₂CH(OH)-(CH₂)₂Bz, m. 92-4° (EtOH). G. M. Kosolapoff

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DM

MARKOVA, Yu.V.; KUZ'MINA, K.K.; SHCHUKINA, M.N.

Synthesis of mercapto amino compounds. Part 2: Synthesis of
11-amino-10-mercaptop heptadecanoic acid and related compounds.
Zhur. ob. khim. 27 no.5:1274-1276 My '57. (MLRA 10:8)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imeni S. Ordzhonikidze.
(Heptadecanoic acid) (Mercapto compounds)

Shchukina, H.N.

Distr: 4E4J/4E2c(j)/4E3d

Synthesis of 2,5- and 2,5'-diphenylhexahydrofuran[3,4-
',4']furan. N. B. Galstukhova and M. N. Shchukina
(S. Ordzhonikidze All-Union Chem.-Pharm. Sci. Research
Inst., Moscow). Zhur. Obschesh. Khim. 27, 1857-65 (1957).
To 3.25 g. LiAlH₄ in 320 ml. Et₂O was added at 0° 8.7 g.
(BzCHCO₂Et)₂ (m. 128-8°) in Et₂O and after 2 hrs. at
20° and 1 hr. at reflux the mixt. was treated with H₂O and
dil. H₂SO₄, yielding 50.4% meso-2,3-bis(α-hydroxybenzyl)-
1,4-butanediol (I), m. 137-8.5° (CICH₂CH₂Cl); tetracetate,
m. 112-13° (EtOH); terabenoate, m. 258-9° (dioxane).
Similar reduction of the isomer of (BzCHCO₂Et)₂, m. 74-8°,
gave dl-2,3-bis(α-hydroxybenzyl)-1,4-butanediol (II), m.
147.6-48° (CICH₂CH₂Cl); tetracetate, m. 143-3.5° (EtOH).
Slow heating of 2.32 g. I with 2 g. KHSO₄ in vacuo to 110-
70° 1 hr. followed by distr. gave 64% 2,5-diphenylhexa-
hydrofuro[3,4-3',4']furan (IIIa), m. 220-30°, m. 88.5-90°
(abs. EtOH), which does not react with Br in CHCl₃ or
with aq. KMnO₄. Similar treatment of II gave 25.6%
2,5-diphenylhexahydrofuro[3,4-3',4']furan, m. 72.5-4.5°
(abs. EtOH). Hydrogenation of these in AcOH over Pd-C
at room temp. and pressure gave, resp., 79% 3,4-dibenzyl-
tetrahydrafuran, m. 85.5-7°, and 49% dl-2,3-dibenzyl-1,4-
butanediol, m. 87-8°. Reduction of dl-dibenzylsuccinic acid
(III) with LiAlH₄ in Et₂O gave 18.3% dl-dibenzyl-1,4-butanediol,
m. 87-8°, identical with above described. III with
EtOH-H₂SO₄ gave 70.9% di-Et ester, m. 80-1.5°, which
treated with LiAlH₄ gave 44.8% dl-2,3-dibenzyl-1,4-butanediol,
m. 87-8°, identical with above described. The diol
forms a diacetate, m. 73.5-4.5° (EtOH). Nitration of IIIa
with HNO₃ (d. 1.5) in AcOH at 20° gave a 2,5-bis(nitro-
phenyl)hexahydrofuro[3,4-3',4']furan, m. 150.5-7.5°
(EtOH). Successful nitration of the 2,5'-diphenyl analog
of IIIa could not be accomplished. Thus, Knorr's (BzCH-
CO₂Et)₂, m. 128-30°, is the meso isomer, while the so-
called γ-isomer, m. 74-8°, is a racemate. G. M. K.

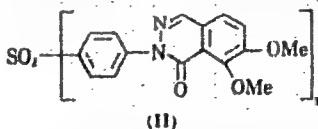
Shechukina, M.M.

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Some derivatives of 4,4'-dihydrazinodiphenyl sulfone and 4-hydrazinophenyl 2-acetamido-5-thiazoyl sulfone. T. V. Gortiuskaya, V. G. Samoilovoya, and M. N. Shechukina (S. Ordzhonikidze All-Union Chem. Pharm. Research Inst., Moscow). Zhur. Obshchei Khim. 27, 1900-1 (1957). Heating 1.4 g. opuntia acid in 50 ml. EtOH with 1 g. (*p*-HCl, H₂NNHC₆H₄)₂SO₂ in 10 ml. H₂O gave a ppt. of 2.2 g. [4-(2,3-d-HO₂C(MeO)₂C₆H₃CH:NNH)C₆H₄)₂SO₂] (I), m. 268-9°. If the reaction is run in H₂O there is formed yellow II, m. 258-60°, which changes to I on heating with ROH or alc. H₂SO₄. Hydrogenation of 4-nitrophenyl-2-amino-5-thiazoyl

4641
4638



sulfone in EtOH over Raney Ni give 87% 4-H₂NC₆H₄ analog, m. 217-19°. Hydrogenation of 4-nitrophenyl-3-acetamido-5-thiazoyl sulfone over Raney Ni in H₂O give the 4-H₂NC₆H₄ analog, m. 208-9°. This (5.4 g.), 42 ml. AcOH, 21 ml. concd. HCl, and 10.6 ml. H₂O diazotized with 1.1 g. NaNO₂ at 0° and the soln. treated with 7.85 g. SnCl₄ in 38.6 ml. HCl, and kept 2 days at room temp. gave 0.3 g. *p*-H₂NNH-C₆H₄ analog HCl salt, m. 222°; the filtrate treated with H₂S and filtered gave with NH₄OH 1.0 g. free base (IIA), m. 243-5°. The following hydrazones are reported: from;

Gorinskaya, T.V.; Sanokova, V.G.; Snetukina, M.N.

(p - $H_3NNHC_6H_4)_2SO_3$ (III) and p - HOC_6H_4CHO , m. 238-40°; from III and p - $AcNHC_6H_4CHO$, m. 262-5°; from III and 3,4-MeO(HO) C_6H_3CHO , m. 250-2°; from 4-hydrazino-phenyl-2-acetamido-5-thiasolyl sulfone (IV) and p - $AcNHC_6H_4CHO$, m. 231-3°; from IV and 3,4-MeO(HO) C_6H_3CHO , m. 238-40°; from IV and opionic acid, m. 203-4°. III showed some *in vitro* activity against human and avian tuberculosis and acid-fast saprophytic sp., *Microsporon* sp., *Trichophyton* sp., *Achorion* sp., and *Ocillomyces* sp. Some activity was found for III hydrazone, p - HOC_6H_4CHO , and IIa.

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4E4

4E3d

PM

SHCHUKINA, M. N.

Distr: 4E4j

Synthesis of some derivatives of β -phenylcysteine. T. P. Sycheva, I. V. Lebedeva, T. Kh. Tsion, and M. N. Shchukina (S. Ordzhonikidze All-Union Chem. Pharm. Research Inst., Moscow). Zhur. Obshchey Khim. 27, 2287-92 (1957); cl. Brown, et al., C.A. 49, 1003b. — Passage of HCl into soln. of phenylcysteine-HCl (I) in abs. EtOH gave the Et ester, m. 140-6°. This with Ph₃CCl in CHCl₃ gave the Et ester of *N*-tritylphenylcysteine, m. 154-6° (EtOH). I treated dropwise to neutral reaction with 18% NaOH gave after air blowing 1 hr. diphenylcystine, decomp. 205-6°. Air blowing of soln. of I Et ester gave diphenylcystine Et ester-HCl, decomp. 191°, which with BzCl gave Et ester of *N,N'*-dibenzoyldiphenylcystine, m. 147-8°. To 3 g. phenylserine Me ester-HCl and 30 ml. AcCl was added slowly 4.5 g. PCl₃ and after shaking 1 hr. the mixt. was chilled overnight yielding 0.6 g. β -chlorophenylalanine Me ester-HCl, decomp. 177° (EtOH-Et₂O). β -Nitrophenylserine Et ester-HCl with BzCl and Na₂CO₃ gave *N*-benzoyl-*p*-nitrophenylserine Et ester, m. 158-9°. Heating 5 g. *N*-benzoylphenylserine Et ester with 1.4 g. P₂S₅ to 110° 1.5 hrs. gave after 8 hrs. at 130° a mass which treated with EtOH, then with H₂O and extd. with Et₂O gave an oil which refluxed 7 hrs. with concd. HCl gave a low yield of $C_{11}H_{12}O_2NS.HCl$, m. 165-6°, which treated with 1% NaOH, and rapidly acidified with AcOH gave 2,5-diphenyl-4-thiaoliniccarboxylic acid, m. 140°. Phenylserine Me ester-HCl and Et₃N in CHCl₃ at 0°, followed by Ph₃CCl gave after 1.5 days at room temp. *N*-tritylphenylserine Me ester, m. 136-8°. To 30 ml. liquid

T.P. SYCHEV, I.V. LEBEDEVA, et al.

NH₃, 2.56 g., I, and 1.23 g. diphenylcysteine was added at -40° 0.9 g. Na, followed by 1.5 ml. MeI and after 2 hrs. the mixt. yielded 2.5 g. S-methylphenylcysteine, m. 163-9°; HCl salt, m. 165-6°. Similar use of BiBr gave S-ethyl-phenylcysteine-HCl, m. 168-70°; the free amino acid, m. 163-4°. Similarly was prep'd. S-butylphenylcysteine, m. 167-9°; HCl salt, m. 155-7°. Attempts to prep. phenylcysteine from chlorochinamic acid and CS(NH₂)₂ failed.

G. M. Kosolapoff

2/2

SHCHUKINA, M.N.; GALSTUKHOVA, N.B.

Letter to the editor. Zhur. ob. khim. 27 no.10:2908 0 '57.
(MIRA 11:4)

(Nitration) (Furan)

79-1-48/63

AUTHORS: Yashunskiy, V. G., Shchukina, M. N.

TITLE: Compounds With Complex-Forming Properties (Veshchestva s kompleksoobrazuyushchey sposobnost'yu) I. Synthesis and Structure of "Complexon IV", i.e. 1,2-Diaminocyclohexane-N,N',N',N'-Tetraacetic Acid (I. Sintez i struktura "Kompleksona - IV" - 1,2-diaminotsiklogeksan-N,N,N',N'-tetrauksusnoy kisloty)

PERIODICAL: Zhurnal Obshchey Khimii, 1958, Vol.28, Nr 1, pp.230-234(USSR)

ABSTRACT: The methods described in publications (references 4, 5, 6) are little applicable to the synthesis of 1,2-diaminocyclohexane-N,N',N',N'-tetraacetic acid (formula I), because they give small yields. The authors worked out a more convenient synthesis of this compound by starting from the accessible dimethyl-(or diethyl)-phthalate. They used Wieland's papers (reference 4) according to which this compound is synthesized from the dihydrazide of cyclohexane-dicarboxylic acid-1,2 (III) according to Curtius. According to the suggested scheme

Card 1/2

79-1-48/63

Compounds With Complex-Forming Properties. I. Synthesis and Structure of "Complexon IV", i.e. 1,2-Diaminocyclohexane-N,N,N',N'-Tetraacetic Acid

the synthesis of "complexon IV" is performed in four stages (the reaction process is given in formulae). The hydrogenation of dimethylphthalate takes place over a nickel catalyst below 50 - 10 atm. at 110 - 140°C without a solvent. On several hours heating the compound (III) is obtained from the hexahydroester with an excess of hydrazine-hydrate. Compound (III) is according to Curtius converted to the dichlorohydrate of 1,2-diaminocyclohexane (II). The final product (I) then results by the influence of monochloroacetic acid upon the dichlorohydrate of diamine in the presence of alkali and in all aspects corresponds to "complexon - IV" described in publications. The authors finally succeeded in proving that this "complexon IV" disposes of a trans- and not a cis-trans-configuration as several scientists had maintained. There are 2 tables, and 9 references, 2 of which are Slavic.

SUBMITTED: December 19, 1956

AVAILABLE: Library of Congress

Card 2/2 1. Chemistry 2. Cyclic compounds-Synthesis

AUTHORS:

Markova, Yu. V., Zenkova, L. N.,
Shchukina, M. N.

SOV/79-28-7-18/64

TITLE:

The Synthesis of Mercapto Amino Compounds (Sintez merkaptoamino-soyedineniy) III. The Synthesis of 3-Mercapto-4-Amino-2-Methylbutane and of 5-Amino-1-Mercapto Pentane (III. Sintez 3-merkapto-4-amino-2-metilbutana i 5-amino-1-merkaptopentana)

PERIODICAL:

Zhurnal obshchey khimii, 1958, Vol 28, Nr 7,
pp 1811 - 1815 (USSR)

ABSTRACT:

The homologs of β -mercaptoproethylamine of the type $R-CH(SH)-CH_2$ have hitherto been little described. For this reason it was of interest to the authors to investigate the influence exerted by the length and the character of the alkyl chain as well as the positions of the functional groups, and to synthesize a number of these compounds. They synthesized for the first time the chlorine hydrate of 3-mercaptopro-4-amino-2-methylbutane, the chlorine hydrate of 5-amino-1-mercaptopentane and its acetyl derivative (see schemes 1 and 2). Already after this work had been completed a paper was published (Ref 3) by Langendorf in which the problems of interest to the authors of the present

Card 1/3

The Synthesis of Mercapto Amino Compounds. III. The SOV/79-28-7-18/64
Synthesis of 3-Mercapto-4-Amino-2-Methylbutane and of 5-Amino-1-Mercapto
Pentane

paper were explained to some extent. In the present paper it was shown that in the hydrolysis of N-benzoyl-5-amino-1-mercaptopentane with hydrochloric acid a partial oxidation of this compound into the corresponding disulfide takes place beside the formation of the chlorine hydrate of 5-amino-1-mercaptopentane. As final product of the oxidation hydrolysis of the chlorine hydrate of N-benzoyl-5-amino-1-isothiuronium pentane the dichlorine hydrate of 5-amino-1-isothiuronium pentane was obtained which did not further hydrolize when heated with alkali liquor. In the oxidation of N-benzoyl-5-amino-1-mercaptopentane with an iodine alcohol solution a bis(N-benzoyl-5-aminopentyl)-disulfide was obtained. A convenient synthesis of N-benzoyl-5-amino-1-chloropentane (in a yield of 63%) was elaborated. There are 10 references, 1 of which is Soviet.

Card 2/3

The Synthesis of Mercapto Amino Compounds. III. The SOV/79-28-7-18/64
Synthesis of 3-Mercapto-4-Amino-2-Methylbutane and of 5-Amino-1-Mercapto
Pentane

ASSOCIATION: Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imeni S.Ordzhonikidze (All-Union Institute of
Scientific Chemical and Pharmaceutical Research imeni S.
Ordzhonikidze)

SUBMITTED: June 27, 1957

1. Butanethiols--Synthesis 2. Pentanethiols--Synthesis

Card 3/3

SHCHUKINA, M.N., prof.; MASHKOVSKIY, M.D., prof.; PERSHIN, G.N., prof., laureat Stalinskoy premii, otv.red.; SERGIYEVSKAYA, S.I., prof., red.; MAGIDSON, O.Yu., prof., laureat Stalinskoy premii, red.; UTKIN, L.M., prof., red.; GROZDEVA, Ye.I., red.; LYUDKOVSKAYA, N.I., tekhn.red.

[Chemistry and medicine] Khimika i meditsina. Otv.red. G.N. Pershin. Moskva, Medgiz. No.9. [Aminazine] Aminazin. 1959.
241 p. (MIRA 12:6)

1. Moscow. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmaceuticheskiy institut. 2. Zaveduyushchaya laboratoriya protivotuberkuleznykh sovedineniy Vsesoyuznogo nauchno-issledovatel'skogo khimiko-farmatsevticheskogo instituta imeni S.Ordzhonikidze (for Shchukina). 3. Zaveduyushchiy laboratoriya otdela farmakologii Vsesoyuznogo nauchno-issledovatel'skogo khimiko-farmatsevticheskogo instituta imeni S.Ordzhonikidze (for Mashkovskiy).

(CHLORPROMAZINE)

SHCHUKINA, M.N., prof.

Preface. Khim.i med. no.11:3-5 '59.
(RADIOACTIVE TRACERS)

(MIRA 13:6)

MAYMIND, V.I.; ZHUKOVA, T.F.; KOSOLAPOVA, N.A.; SHCHUKINA, M.N.

Synthesis of S^{35} -methionine. Khim.i med. no.11:9-14 '59.
(MIRA 13:6)
(METHIONINE)

POZHARSKAYA, A.M.; ZHUKOVA, T.F.; SHCHUKINA, M.N.

Synthesis of D-cysteine-S³⁵. Khim.i med. no.11:14-17 '59.
(MIRA 13:6)
(CYSTEINE)

MARKOVA, Yu.V.; ZHUKOVA, T.F.; SHCHUKINA, M.N.

Synthesis of S³⁵-carbon disulfide. Khim. i med. no.11:26-29
'59. (MIRA 13:6)
(CARBON DISULPHIDE)

MARKOVA, Yu.V.; ZENKOVA, L.N.; SHCHUKINA, M.N.

Synthesis of S^{35} -thiamine. Khim.i med. no.11:29-34 '59.
(MIRA 13:6)
(THIAMINE)

PEEDVODITELEVA, G.S.; SHCHUKINA, M.M.

Synthesis of S³⁵-aminazine. Khim. i med. no.11:34-39 '59.
(MIRA 13:6)
(CHLORPROMAZINE)

MARKOVA, Yu. V.; KUZ'MINA, K.K.; SHCHUKINA, M.N.

Synthesis of S³⁵-merkamin. Khim. i med. no.11:39-42 '59.
(MIRA 13:6)
(ETHANETHIOL)

MARKOVA, Yu.V.; ZENKOVA, L.N.; SHCHUKINA, M.N.

New method for the synthesis of C^{14} -paraaminobenzoic acid and
obtaining C^{14} -anesthesin, novocaine, and cocaine. Khim.i med.
no.11:53-59 '59. (MIRA 13:6)

(BENZOIC ACID)

(ANESTHETICS)

MARKOVA, Yu.V.; ZENKOVA, L.N.; SHCHUKINA, M.N.

Synthesis of barbiturates labeled with C¹⁴ and S³⁵. Khim.i med.
no.11:60-68 '59. (MIRA 13:6)
(BARBITURATES)

SYCHEVA, T.P.; LEBEDEVA, I.V.; SHCHUKINA, M.N.

Model synthesis of C¹⁴-dimedrol. Khim.i med. no.11:77-82 '59.
(MIRA 13:6)
(DIPHENHYDRAMINE)

SAMOLOVOVA, V.G.; YERMOIAYEVA, V.G.; GORTINSKAYA, T.V.; YASHUNSKIY, V.G.;
SHCHUKINA, M.N.

Synthesis of asterol and other derivatives of aminotoxibenzthiazoles.
Med. prom. 13 no.5:23-26 My '59. (MIRA 12:?)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmaceuticheskiy
institut imeni S. Ordzhonikidze.
(THIAZOLE)

PREDVODITELEVA, G.S.; SHCHUKINA, M.N.

New variant of diacarb synthesis. Med.prom. 13 no.9:24-26 S '59.
(MIRA 13:1)
1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imeni S. Ordzhonikidze.
(THIADIAZOLE SULFONAMIDE)

7 (4)
AUTHORS:

Chao Erh-chang, nichukina, M. N.

S07/79-29-3-56/61

TITLE:

Synthesis of the Dialkyi-amino-alkyl-derivatives of Indazol
(Sintez dialkilaminoalkil'nykh proizvodnykh indazola)

PERIODICAL:

Zhurnal obshchey khimii, 1959, Vol 29, Nr 3, pp 1012-1020 (USSR)

ABSTRACT:

The authors carried out the synthesis of the above mentioned compounds in order to investigate their chemical, pharmaceutical, and antibacterial properties since the dialkyi-amino-alkyl grouping plays an important role in the pharmaceutical products. Many synthetic spasmolitic anaesthetic anti-malaria remedy and others contain this grouping which is connected with a nitrogen- or oxygen atom. For this reason it was interesting to synthesize compounds of such a type in the series of indazol (which is according to its structure assumed to be an isostere of indol and an isomer of benzimidazole) which are as heterocycles ingredients of the biologically important products. The N-diethyl-amino-ethyl-6-nitroindazol was synthesized with a good yield by the condensation of the 6-nitro-indazol with diethyl-amino-ethylchloride in the presence of sodium alcoholate. The N-dimethyl-amino-ethyl-6-nitroindazol, N-dimethyl-amino-ethyl-3-chloroindazol and N-dimethyl-amino-

Card 1/3

SOV/79-29-3-56/61

Synthesis of the Dialkyl-amino-alkyl-derivatives of Indazol

ethyl-indazol were obtained by the same method. Since the free base of dimethyl-amino-ethyl chloride polymerizes easily in the case of distillation its hydrochloride and the double quantity of alcoholate were introduced into the reaction. In the case of the indazol the yield is smaller than in the case of 6-nitro- and 3-chloroindazol which may be explained by the presence of chlorine and the nitrogroup which draws off the electrons. This increases the activity of the hydrogen atom at the nitrogen (Scheme). In the case of the alkylation of indazol and its derivatives (Ref 1), as well as in the case of its condensation with dialkyl-amino-alkyl chlorides 1- and 2-derivatives are formed. Thus the 1- and 2-diethyl-amino-ethyl- and dimethyl-amino-ethyl derivatives of the 6-nitroindazol, 6-aminoindazol and 3-chloro-6-nitroindazol, the 1- and 2-dimethyl-amino-ethyl indazols, and the 1- and 2-dimethyl-amino-ethyl-3-chloroindazols as well as the 2-diethyl-amino-ethyl-6-oxyindazol were obtained. The separation of the mixtures of the 1- and 2-isomers was obtained by fractionated crystallization of the hydrochlorides or by the fractionated precipitation of the picrates. The structure was proved by comparison with the spectral analysis. There are 4 figures and 10 references.

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SOV/79-29-3-56/61

Synthesis of the Dialkyl-amino-alkyl-derivatives of Indazol

ASSOCIATION: Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut (All-Union Scientific Research Institute of Chemical Pharmacy)

SUBMITTED: January 8, 1958

Card 3/3

5(3)

SOV/79-29-6-59/61

AUTHORS: Yashunskiy, V. G., Vasil'yeva, V. F., Tikhonova, L. I.,
Shchukina, M. N.

TITLE: Substances With a Complex-forming Capacity. IV. Trans-1,2-di-
aminocyclohexene- and 1-Phenylethylenediamine-N,N,N',N'-tetra-
acetic Acids

PERIODICAL: Zhurnal obshchey khimii, 1959, Vol 29, Nr 8,
pp 2709 - 2712 (USSR)

ABSTRACT: The authors previously reported on the synthesis and investigation of the complex-forming capacities of some alicyclic 1,2-diaminetetraacetic acids of a trans-configuration (Refs 1,2). In order to complement this series the compound (I) was synthesized. The initial product for the synthesis of this compound was the dimethyl ester of the cis-cyclohexene-(4)-dicarboxylic acid-1,2 obtained by the condensation of butadiene with the anhydride of maleic acid. When this cis-diester is heated with hydrazine hydrate without solvent the trans-dihydrazide forms (Ref 1). The latter was transformed according to Curtius into the dichlorohydrate of the hitherto

Card 1/3

Substances With a Complex-forming Capacity. IV.

SOV/79-29-8-59/81

Trans-1,2-diaminocyclohexene- and 1-Phenylethylenediamine-N,N,N',N'-tetraacetic Acids

unknown trans-1,2-diaminocyclohexene-(4) which was treated with an excess of chloroacetic acid in an alkaline medium which led to the compound (I). In order to investigate the influence of the substitutes on the complex-forming capacity of the complexes of the ethylenediaminetetraacetic acid series the compound (II) obtained from 1,2-diaminoethylbenzene by two different methods was synthesized (Ref 3, and Rodionov, Ref 4). The tetraacetic acid could only be synthesized by heating 1,2-diaminoethylbenzene with an excess of bromoacetic acid in the presence of caustic soda at 40°. Thus two compounds hitherto not described were synthesized: trans-1,2-diaminocyclohexene-(4)-, and 1-phenylethylenediaminetetraacetic acid. The complex-forming capacity of the synthesized compounds was determined chromatographically (Ref 5) by way of comparison with ethylenediaminetetraacetic acid. By this method it was shown that the new complexes have a complex-forming capacity of the same order as ethylenediaminetetraacetic acid. The table shows the result of these chromatographic determinations.

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Substances With a Complex-forming Capacity. IV. SOV/79-29-8-59/81
Trans-1,2-diaminocyclohexene- and 1-Phenylethylenediamine-N,N,N',N'-tetra-
acetic Acids

The results of the investigation of complexon (II) show that the presence of the phenyl radical beside one of the amino groups of ethylenediaminetetraacetic acid has but little effect upon the complex-forming capacity. There are 1 table and 6 references, 5 of which are Soviet.

SUBMITTED: July 5, 1958

Card 3/3

5 (3)

AUTHORS: Murav'yeva, K. M., Shchukina, M. N. SOV/20-126-6-36/67

TITLE: Synthesis and Regroupings in the Series of Thiazoline Imine
(Sintez i peregruppirovki v ryadu tiazolinimina)PERIODICAL: Doklady Akademii nauk SSSR, 1959, Vol 126, Nr 6, pp 1274 - 1277
(USSR)ABSTRACT: In the condensation of thiourea or of its substituents with α -halogen carbonyl compounds derivatives of the 2-amino-thiazole or thiazoline imine are formed. In the present paper the authors investigated the condensation of the α -halogen ketones with symmetric diaryl and aryl-acyl urea as well as the regroupings of the cyclic compounds obtained. It was found that the reaction course depends on the presence of the hydrogen ions in the reaction medium. If the forming halogen hydrogen is linked by triethylamine, 4-oxy-thiazolidine derivatives are formed. In aqueous or alcoholic HCl solution they cleave-off water. The intermediate compounds are unstable especially if they were produced from diaryl thiourea (Table 1, I a). In the condensation of the symmetric ditolyl and diphenetidyl-thiourea with acetone chloride the authors directly obtained 2-tolyl-imino-3-tolyl-4-methyl-thiazoline (II) and 2-p-ethoxy-phenyl-

Card 1/4

Synthesis and Regroupings in the Series of Thiazoline SOV/20-126-6-36/67
Imine

-imino-3-p-ethoxy-phenyl-4-methyl-thiazoline (III) without intermediate compounds. Intermediate products in the condensation of the α -halogen ketones with N-aryl-N'-acyl-thiourea show a stronger stability. They cleave-off water in the action of HCl in the cold, and pass over into the corresponding thiazoline compounds, which in most cases strongly differ by their melting temperature (IV-IX). The acyl-imino-thiazolines (IV, V, VI) produced by the authors are saponified with HCl by a short heating into 2-imino-3-phenyl-4-methyl-thiazoline (Ref 5). By boiling this imine (or IV, V, VI) for several hours with HCl a regrouping and a formation of 2-phenyl-amino-4-methyl-thiazole (Ref 6) take place. The compound VII was saponified to a 2-imino-3,4-diphenyl-thiazoline (Ref 5). After a long boiling with HCl this imine showed a regrouping and yielded 2-phenyl-amino-4-phenyl-thiazole (Refs 5,7). In the heating of ω -bromo acetophenone and phenyl acetyl thiourea in an absolute alcoholic solution, 2-acetyl-imino-3,4-diphenyl-thiazoline-4 was produced (VIII). This compound is saponified into 2-imino-3,4-diphenyl-thiazoline-4. However, ω -bromo acetophenone as well as phenyl acetyl thiourea form the oxy compound IVa. Thus in the reaction course

Card 2/4

Synthesis and Regroupings in the Series of Thiazoline SOV/20-126-6-36/67
Imine

benzoyl as if from the methylene group migrates to the nitrogen of the thiourea, while acetyl migrates from this nitrogen atom to the methylene group. The compounds IX, X and XI are saponified to 2-imino-3-phenyl-4,5,6,7-tetra-hydro-benzthiazoline (XII) in heating with 20% HCl. This substance is transformed into 2-phenyl-amino-4,5,6,7-tetra-hydro-benzthiazole (Ref 8) by boiling during several days with 20% HCl. The authors explain the above transformations by the following: The thiourea substituents enter in their isoform the reaction with α -halogen ketones by forming S- β -keto-substituents of the isothioureas. They are still subject to further transformations. The carbonyl oxygen captures a proton from the aminophenyl residue which brings about a formation of an N-C-bond. 4-oxy-thiazolidine compounds are formed which readily cleave-off water. The regrouping of the 2-imino-3,4-substituents of thiazoline in boiling with HCl may be explained by the addition of a proton to the nitrogen of the ring, by the rupture of the 3,4-bond and by the resulting polarization of the molecule. The cycle is then closed at the nitrogen of the imino group and 2-phenyl-amino-4-substituted thiazoles are formed. The reactions investigated show that

Card 3/4

Synthesis and Regroupings in the Series of Thiazoline SOV/20-126-6-36/67
Imine

the condensation of the α -halogen ketones with N-phenyl-N'-acyl-thiourea passes over the stage of the 4-oxy-thiazolidine derivatives. These compounds are, similar to the 2-imino-thiazolines-4, very unstable and have the tendency towards regroupings which bring about the rupture of the heterocycle. There are 1 table and 8 references, 2 of which are Soviet.

ASSOCIATION: Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut im. S. Ordzhonikidze (All-Union Scientific Chemo-pharmaceutical Research Institute imeni S. Ordzhonikidze)

PRESENTED: February 24, 1959, by I. L. Knunyants, Academician

SUBMITTED: February 19, 1959

Card 4/4

RUBTSOV, M.V., prof., otv. red.; PERSHIN, G.N., prof., zam. otv. red.; MAGIDSON, O.Yu., prof., red.; MASHKOVSKIY, M.D., prof., red.; UTKIN, L.M., prof., red.; RYZHENTSEVA, A.K., prof., red.; SHCHUKINA, M.N., prof., red.; BAYCHIKOV, A.G., kand. tekhn. nauk, red.; MIKHALEV, V.A., kand. khim. nauk, red.; RYAZANTSEV, M.D., kand. tekhn. nauk, red.; Suvorov, N.N., kand. khim. nauk, red.; ILYASHKEVICH, A.M., st. nauchnyy sotr., red.

[Basic trends in the work of the S.Ordzhonikidze All-Union Chemico-pharmaceutical Scientific Research Institute; survey of its activity from 1920 to 1957] Osnovnye napravleniya rabot VNIKhFI; obzor deiatel'nosti za 1920-1957 gg. Moskva, 1959. 649 p. (MIRA 15:5)

1. Moscow. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut.
(CHEMISTRY, MEDICAL AND PHARMACEUTICAL)

SYCHEVA, T.P.; LEBEDEVA, I.V.; SHCHUKINA, M.N.

Reaction of α -methylthiazole with sulfur and amines. Zhur.
VKHO 5 no. 2:234-235 '60. (MIRA 14:2)

1. Nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imen Sergo Ordzhonikidze.
(Thiazole) (Sulfur) (Amines)

SYCHEVA, T.P.; KUZ'MICHEVA, T.P.; CHERNYAYEVA, A.T.; TRUPP, T.Kh.;
SHCHUKINA, M.N.

Synthesis of apressin. Med.prom. 14 no.2:13-17 F '60.

(MIRA 13:5)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imeni S. Ordzhonikidze.

(PHTHALAZINE)

GALSTUKHOVA, N.B.; SHCHUKINA, M.N.

Synthesis of etoxide, a new antituberculosis drug. Med. prom. 14
no.8:15-18 Ag, '60. (MIRA 13:8)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut im. S. Ordzhonidze.
(CARBANILIDE)

GORTINSKAYA, T.V.; SHEINA, N.P.; SHCHUKINA, M.N.

Determination of the dissolution properties and the mechanical hardness
of tablets. Materials for the 9th edition of the State Pharmacopoeia
of the U.S.S.R. Med. prom. 14 no.9:15-23 S '60. (MIRA 13:9)
(TABLETS (MEDICINE))
(DRUG INDUSTRY--EQUIPMENT AND SUPPLIES)

GORTINSKAYA, T.V.; SHEINA, N.P.; SHCHUKINA, M.N.

Some derivatives of 3-methoxy-6-(sulfanilamido)-pyridazine. Med.
prom. 14 no.9:23-25 S '60. (MIRA 13:9)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imeni S. Ordzhonikidze.
(PYRIDAZINE)

SIMCHUKINA, N.N.

Synthetic drugs produced by a number of French pharmaceutical firms.
Med. prom. 14 no. 10:57-62 6 '60. (MIRA 13:10)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imeni S. Ordzhonikidze.
(FRANCE--DRUGS)

ZHEREBCHENKO, P.G.; GOLOVCHINSKAYA, Ye.S.; KOSTYANOVSKIY, R.G.; KRASNYKH,
I.G.; KUZNETS, Ye.I.; MAGIDSON, O.Yu.; MURASHOVA, V.S.; PASTUKHOVA,
I.S.; PRISOBRAZHENSKAYA, M.N.; SUVOROV, N.N.; TER-VARTANYAN, L.S.;
ZHKKHINVADZE, K.A.; SHASHKOV, V.S.; SHCHUKINA, M.N.

Role of oxidative deamination in the mechanism of radiation
protection afforded by some amines. Zhur. ob. biol. 21 no.2:
157-160 Mr-Ap '60.

(MIRA 13:6)

(RADIATION PROTECTION) (DEAMINATION)

SEARCHED
INDEXED - 10

ATTACHED: S. J. K. T. P., Shandor, M. F.

AFFILIATE: Some Phthalazine Derivatives with Potential Chemotherapeutic Activity

PERIODICAL: Zhurnal Organicheskoy Khimii, 1970, Vol. 6, No. 6, pp. 133-141 (JOCR)

ABSTRACT:
Card 1 of 3

This article deals with some phthalazine derivatives and their effectiveness against the tuberculosis bacillus. 1-(*p*-nitrophenyl)-3-phenyl-4-phthalazinone and its analogs with nitro, amino, and hydroxyl groups in para position on the phenyl radical, were synthesized in numbers to investigate their therapeutic activity. Phenyl- and *p*-nitrophenylhydrazines with phthalic anhydride yielded the corresponding 1,4-diketo-3-aryltetrahydropthalazines which were subsequently alkylated. Catalytic hydrogenation of 1-(*p*-nitrophenyl)-3-(*p*-nitrophenyl)-phthalazone gave the corresponding amine, which was converted into its acetate derivative. Since 1-hydrazinophthalazine is

Chemical Department, Institute of
Pharmacology and Toxicology

Sov. 79-31-0070

Chemical synthesis, the hydrochloride with characteristic
antitubercular compounds of sulfone, p-phenylbenzene-
sulfonyl, and p-dimethylaminobenzylidene were synthesized.
Some derivatives of the phthalimide carboxylic acid were
also obtained. Most of the synthesized compounds, with
the exception of 2,6-diaminocyclohexyl-4-phthalimidine,
had no appreciable activity against tubercle bacilli.
Card No. 37

Card No. 37
Serum, and i.p. to 10,000 with serum. In experimental
tuberculosis treatment of white mice, the compound was
found to be totally inactive. Biological research was
conducted under the supervision of G. N. Perskin at
the chemotherapy department of the S. A. Vichkanyev All-
Union Chemical and Pharmaceutical Scientific Research
Institute. There are 11 references, 4 Swiss, 3 U.K., 1 U.S.,
1 French, 1 Soviet, 1 German. The U.S. and U.K. refer-
ence: E. Berlin, D. Drulin, et al., J. Pharm. Pharmac., 1955,
4, 11, 114; D. Drulin, D. Segal, J. Chem. Soc., 1955,

1, 1, 1; F. Klem, J. Gaffin, A. Peters, J. Chem. Soc., 1950, 22, 255; M. J. J. Kowalski, F. Gregory, et al., Proc. Soc. Exp. Biol. Med., 79, 563 (1952).

ASSOCIATION: S. Grushnikov's All-Union Chemical and Pharmaceutical Scientific Research Institute (Vsesoyuznyy nauchno-issledovatel'skyy khimiko-farmatsevicheskiy institut imeni S. Grushnikova)

SUBMITTED: February 1, 1968

4380

1000
1977-10-10/17

AUTHORS: Vasil'eva, V. F., Meshunkov, V. G., Shchekina,
M. N.

TITLE: Letters to the Editor. Concerning the Reaction of
Sydnone With Derivatives of α , β -Unsaturated
Acids

PERIODICAL: Zhurnal obshchei khimii, 1979, Vol 49, No 2,
p 415 (USSR)

ABSTRACT: Sydnone on heating with nitriles and esters of
 α , β -unsaturated acids undergo cleavage and
yield derivatives of pyrazoline and pyrrole,
accompanied by evolution of the carbon dioxide.
When the reaction of sydnone with unsaturated
esters yields esters of substituted pyrazolin-
one-phosphoric acids, the reaction of sydnone with
nitriles yields only substituted pyrroles. In
both cases, probably, the formation of esters or
nitriles of substituted pyrazoline-phosphoric acids
takes place. However, the cyano group in these

Card 1/3

Latters to the Editor. I have written the
Reaction of Acrylonitrile with Derivatives
of α, β -Unsaturated Ketones

100/100-100/100

concerning the ability of acrylonitrile to
effect the conversion of phenylpropanone into
"crown" addition products.



Acrylonitrile; R. J. P. Williams, U.S. Pat. No.

This publication of my letter to you concerning
the ability of acrylonitrile to effect the
conversion of phenylpropanone into
"crown" addition products, is
published now in the reaction of acrylonitrile
and α -cyanocinnamone, formed the same
substituted nitrogen compound. Heating β -phenylacrylonitrile
with excess acrylonitrile yields 1-phenylpyrrole
(yield 80%). The structure of the obtained com-
pounds was confirmed by spectral analysis, as well
as by comparison with literature data. There is 1
German reference.

Card 2/3

Letters to the Editor. Concerning the
Reaction of Sydnone With Derivatives
of α , β -Unsaturated Acids

77324
SOV/TB-50-4-75, '56

ASSOCIATION: S. Ordzhonikidze All-Union Scientific Research Chemical
and Pharmaceutical Institute (Vsesoyuznyy nauchno-
issledovatel'skiy khimiko-farmatsevticheskiy institut
imeni S. Ordzhonikidze)

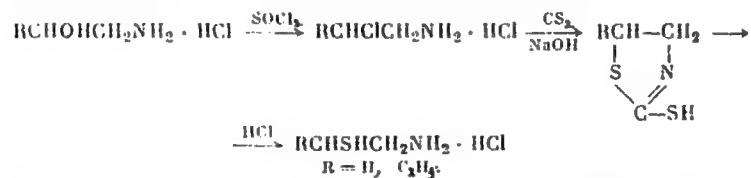
SUBMITTED: October 26, 1959

Scanned by

Card 1/4

7307
SOV/70-3-61/69

AUTHORS: Markova, Yu. V., Kuz'mina, K. K., Shchukina, M. N.

TITLE: Synthesis of Mercaptoamino Compounds. IV. Synthesis of β -Mercaptoethylamine and 1-Amino-2-mercaptopbutanePERIODICAL: Zhurnal obshchei khimii, 1960, Vol 30, Nr 3,
pp 1039-1043 (USSR)ABSTRACT: This paper describes synthesis of β -mercaptoethylamine and 1-amino-2-mercaptopbutane according to the scheme used previously for synthesis of 3-mercpto-4-amino-2-methylbutane (Yu. V. Markova, L. N. Zenkova, M. N. Shchukina, ZhOKh, 28, 1811 (1958)):

Card 1/4

Synthesis of Mercaptoamino Compounds. IV

78307
SOV/79-30-3-61/69

β -Mercaptoethylamine hydrochloride (I) was obtained (42%, based on the initial ethylamine) as follows: a mixture of 2-mercaptopthiazoline and HCl (20% solution) was boiled for 50 hours on an oil bath; the mixture was evaporated under vacuum and dissolved in absolute alcohol; the alcoholic solution, to which charcoal had been added, was warmed and filtered; absolute ether was added to the filtrate and left to stand for 24 hr.

The precipitate was removed by filtration. I has mp 67-69°; 2-mercапто-1-aminobutane hydrochloride (II) was obtained (50%) by the same method as I; it has mp 134-138°.

There are 10 references, 1 U.S., 5 German, 2 Swiss, 2 Soviet. The U.S. reference is: R. H. Haal, F. Wright, J. Am. Chem. Soc., 73, 2215 (1951).

ASSOCIATION: S. Ordzhonikidze All-Union Chemical-Pharmaceutical Scientific Research Institute (Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze)

SUBMITTED: December 27, 1958

Card 2/2

SAMOLOVOVA, V.G.; GORTINSKAYA, T.V.; SHCHUKINA, M.N.

Phenoxazine. Part 1: Synthesis of some 10-substituted derivatives
of phenoxazine. Zhur.ob.khim. 30 no.5:1516-1517 My '60.
(MIRA 13:5)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imeni S.Ordzhonikidze.
(phenoxazine)

GORSHINSKAYA, T.V.; SHCHUKINA, M.N.

Some derivatives of pyridazine. Zhur.ob.khim. 30 no.5:
1518-1520 My '60. (MIRA 13:5)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imeni S.Ordzhonikidze.
(Pyridazine)

PREDVODITELEVA, G.S.; SHCHUKINA, M.N.

Studies in the phenoxazine series. Part 2: Synthesis of
some derivatives of substituted 1-phenoxazinecarboxylic acid.
Zhur.ob.khim. 30 no.6:1893-1897 Je '60.
(MIRA 13:6)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevti-
cheskiy institut imeni S. Ordzhonikidze.
(Phenoxazine) (Phenoxazinecarboxylic acid)

MURAV'YEVA, K.M.; SHCHUKINA, M.N.

Synthesis and rearrangements in the thiazoline imine series.

Part 1: Condensation of chloroacetone and -chlorocyclohexanone with sym. diaryl- and arylacylthioureas. Zhur.ob. khim. 30 no.7:2327-2334 Jl '60. (MIRA 13:7)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(Acetone) (Cyclohexanone) (Urea)

MURAV'YEVA, K.M.; SHCHUKINA, M.N.

Synthesis and rearrangements in the thiazoline imine series.
Part 2: Condensation of ω -bromoacetophenone with N-phenyl-N'-acylthioureas. Zhur.ob.khim. 30 no.7:2334-2340 J1 '60.
(MIRA 13:7)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(Urea) (Acetophenone)

MURAV'YEVA, K.M.; SHCHUKINA, M.N.

Synthesis and rearrangements in the thiazoline imine series.
Part 3: Rearrangement of 2-imino-3-phenyl-4-thiazolines into
2-phenylaminothiazoles. Zhur.ob.khim. 30 no.7:2340-2343
J1 '60. (MIRA 13:7)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(Thiazoline) (Thiazole)

MURAV'YEVA, K.M.; SHCHUKINA, M.N.

Synthesis and rearrangements in the thiazoline imine series.
Part 4: Effect of acetylating agents on 2-acylimino-4-hydroxythiazolidines. Zhur.ob.khim. 30 no.7:2344-2348
Jl '60. (MIRA 13:7)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S.Ordzhonikidze.
(Thiazolidine)

BANASHEK, A.; SHCHUKINA, M.N.

β - And γ -pyridylthiazolines. Zhur.ob.khim. 30 no.10:3328-3332
0 '61. (MIRA 14:L)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imeni S.Ordzhonikidze.
(Thiazoline)

S/079/60/030/012/008/027
E001/B064

AUTHORS: Yashunskiy, V. G., Smolin, D. D., Yermolayeva, V. G.,
and Shchukina, M. N.

TITLE: Substances Capable of Complex Formation. V. 2,2'-Diamino-diethyl Ether-N,N,N',N'-tetraacetic Acid

PERIODICAL: Zhurnal obshchey khimii, 1960, Vol. 30, No. 12,
pp. 3916-3918

TEXT: The authors continue their studies (Ref. 2) of the synthesis of complexes by synthesizing 2,2'-diamino-diethyl ether-tetraacetic acid; this synthesis has hitherto not been described. It may, however, be assumed that this complex was obtained on the basis of data of an English patent (Ref. 3) from 2,2'-diamino-diethyl ether by carboxymethylation. Several experiments had failed before the complex was obtained by reacting 2,2'-diamino-diethyl ether. The diamino ether was obtained from 2,2'-dichloro diethyl ether with the diphthalimide derivative by the reaction of Gabriel (Ref. 4), however, the 2,2'-di(phthalimido)-diethyl ether was split off by boiling with an alcohol solution of hydrazine hydrate and subsequent treatment with hydrochloric acid which simplified the reaction and led to an

Card 1/2

Substances Capable of Complex Formation.
V. 2,2'-Diamino-diethyl Ether-N,N,N',N'-
tetraacetic Acid

S/079/60/030/012/008/027
B001/B064

abruptly increasing yield. The diamine was separated as dichloro hydrate and reacted with monochloro acetic acid. The reaction was normal and took place in alkaline medium (Ref. 2). Since it was not possible to precipitate tetra acid by acidifying the reaction mass, which is the case with some other complexons, two methods of precipitation were applied. The cationite KU-2 was used for the first one applied in the study of Ref. 5. By the latter method the reaction mixture was acidified until the acid reaction toward Congo red as indicator had been reached and, after the separation of sodium chloride from the solution, the monosodium salt of the complexon precipitated with methanol and purified by repeated precipitation with methanol from water. There are 6 references: 2 Soviet, 1 US, 1 Swiss, 1 German, and 1 British.

ASSOCIATION: Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy institut imeni S. Ordzhonikidze (All-Union Chemical and Pharmaceutical Scientific Research Institute imeni S. Ordzhonikidze)

SUBMITTED: January 11, 1960

Card 2/2

SYCHEVA, T.P.; SHCHUKINA, M.N.

Reaction of 2-methyloxazole with sulfur and amines. Zhur.VKHO
6 no.1:117-118 '61. (MIRA 14:3)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut im. S.Ordzhonikidze.
(Oxazole) (Amines) (Sulfur)

SHCHUKINA, M.N.

Modern antituberculosis drugs. Med. prom. 15 no. 4:13-25 Ap '61.
(MIRA 14:4)

l. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imeni S. Ordzhonikidze.
(TUBERCULOSIS—PREVENTION) (DRUGS)

YASHUNSKIY, V.G.; SHCHUKINA, M.N.; YERMOLAYEVA, V.G.; SAMOYLOVA, O.I.

Synthesis of imizine hydrochloride, N-(3-dimethylaminopropyl)-
iminodibenzyl. Med. prom. 15 no.12:10-13 D '61. (MIRA 15:2)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imeni S. Ordzhonikidze.
(IMIPRAMINE)

SYCHEVA, T.P.; NEKHLIN, Ya.G.; SICHUKINA, M.N.

Synthesis of phenizine. Med. prom. 15 no.12:14-17 D '61.

(MIRA 15:2)

1. Vsesoyuznyy nauchno-issledovatel'skiy khimiko-farmatsevticheskiy
institut imeni S. Ordzhonikidze.
(HYDRAZINE)